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Diagnostic Clues in Metastatic Lesions of Endocarditis in Addicts

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Gram stains and cultures of multiple extravascular sites showed the infecting organisms in 17 of 26 heroin addicts with endocarditis. In addition to routine blood cultures, the etiologic agent was cultured from Osler nodes and Janeway lesions in ten patients, subcutaneous abscesses in eight, pleural fluids in eight, joint aspirates in three, spinal fluids in three, pericardial fluids in two, muscle abscesses in two and endometrium in one patient. Gram-positive cocci were found in extravascular lesions in 11 of 12 patients with staphylococcal endocarditis and from as many as four different sites. In contrast, no Gram-positive cocci were seen in extravascular sites in any of eight patients with enterococcal endocarditis although six of them had peripheral lesions. Gram stain and culture of multiple extravascular sites appears to provide a valuable early clue to the nature of the etiologic agent in addict endocarditis.

IN MANY MEDICAL CENTERS the incidence of addict endocarditis now far exceeds that of classical subacute bacterial endocarditis. The clinical features of these two forms of endocarditis differ; therefore an altered approach both to diagnosis and to management is warranted. In spite of changing patterns, a murmur and a positive blood culture remain as the two imperative criteria for the diagnosis of bacterial endocarditis. In this respect, addict endocarditis may be atypical in that the onset of murmurs is often delayed for many days after a patient is admitted to hospital because of illness. We have found that in many

patients later proven to have bacterial endocarditis, aspiration with Gram stain and culture of several extravascular "metastatic sites" provides clues helpful to both diagnosis and management.

Patients and Methods

During 18 months (July 1973 through December 1974), 26 cases of endocarditis were diagnosed in heroin addicts. In 22 patients the diagnosis was evident at the time of admission or at initial consultation. In four patients, however, the diagnosis resulted from bacterial growth in routine blood cultures obtained, before admission, from a group of 37 patients admitted for heroin detoxification.² At least three sets of blood cultures obtained later were also positive. The patients were afebrile and had no pulmonary lesions. In all instances, the diagnosis was confirmed by

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characteristic physical findings and results of procedures including cardiac catheterization (7 patients), echocardiography (17 patients), angiography (5 patients), surgical operation (6 patients) and autopsy (3 patients). Multiple sets of blood cultures were positive in all of the 26 patients. Blood culture reports were available at the time of initial consultation in only four patients.

A careful search was made in all patients for Osler nodes, Janeway lesions and subcutaneous abscesses. For the purposes of definition, all erythematous, painful and tender nodular lesions, a few millimeters to a centimeter in size with a somewhat pale center, on the palmar and plantar surface of hands and feet and the tips of fingers and toes were considered as Osler nodes.³ Those that were not painful were considered as Janeway lesions.⁴ Similar lesions on other areas of the body, such as the chest and abdomen, are simply described as subcutaneous abscesses. For control, a smear from adjacent normal skin was also Gram-stained on the same slide. The skin lesions, including Osler and Janeway lesions, were considered positive if the Gram-stained slide prepared from the needle aspirate of the lesion, when examined under oil immersion, showed the presence of both polymorphonuclear leukocytes and bacteria at least once in every three to four fields. They were considered positive when the material aspirated from the lesions had a greater number of bacteria than from the adjacent uninvolved skin used as control.

Gram stain and cultures were done on fluids obtained from Osler, Janeway and other skin lesions; transtracheal aspirates, and aspiration of pleural, spinal and pericardial fluids; results were later correlated with blood culture findings. The criteria for a diagnosis of bacterial endocarditis were (1) at least four sets of positive blood cultures, (2) clearly audible murmurs either on admission or appearing within ten days, (3) fever greater than 38.3°C (101°F) and (or) (4) evidence of metastatic lesions—that is, roentgenographic evidence of pneumonia, cutaneous lesions, microscopic hematuria and a palpable spleen. These criteria were satisfied in all 26 patients. *Staphylococcus aureus* was identified by colony morphology, coagulase reaction and growth on mannitol-salt agar. Enterococci were identified by gamma hemolysis on the blood agar plates, growth on 40 percent bile, esculin hydrolysis and growth in 6.5 percent salt broth.

Results

Clinical Features

Fourteen men and 12 women aged 21 to 55 were admitted with anemia (85 percent), fever (77 percent), leukocytosis (65 percent). A third of them had no audible murmurs on admission and an additional 15 percent were totally asymptomatic, admitted for detoxification. Eleven patients (42 percent) had left-sided and eight (31 percent) had right-sided endocarditis. Seven patients had endocarditis on both sides. The mitral valve was involved in 12 (46 percent), tricuspid in 10 (38 percent), aortic in 8 (31 percent) and pulmonary in 4 (15 percent). Fifteen patients had pneumonia and eight had empyema. Only four (15 percent) had a palpably enlarged spleen. Seven (27 percent) patients had neurological symptoms such as hemiplegia in five (19 percent), polyneuritis in two (8 percent) and blindness in one (4 percent) (one patient had both polyneuritis and blindness).

Mode of Onset

Endocarditis was the admitting diagnosis in only four out of 26 patients. As noted, four patients were asymptomatic upon admission and were discovered to have endocarditis by routine blood cultures drawn before admission to hospital for detoxification. Bizarre and confusing presentation was not unusual and, in several patients, the initial clinical picture was quite misleading. An extreme example was a young woman with *Serratia marcescens* endocarditis who was admitted to hospital with suprapubic pain, fever and chills thought to be septic abortion and endometritis. Her lochia was initially reddish in color and this was attributed to altered blood; culture of endometrium yielded a heavy growth of *S. marcescens*. This organism was also isolated from blood for ten days after curettage and antibiotic therapy. Congestive heart failure was the presenting feature in a diabetic patient, later found to have polymicrobial endocarditis due to *Lactobacillus* and *Enterococcus*. All positive culture sources will be described under two categories: intravascular and extravascular.

Intravascular Culture Sites

Staphylococcus aureus was the most frequent causative organism and was isolated from 12 (46 percent) patients. *Enterococcus* was the second most common pathogen and was recov-

with enterococcal endocarditis, sudden onset of monoparesis developed, but the spinal fluid cultures were negative.

Pneumonia or pleural effusion (or both) was the presenting feature in nearly half of the cases. Pleural aspirates in eight patients showed Gram-positive cocci (*S. aureus*) in seven and Gram-negative rods (*Pseudomonas aeruginosa*) in one. Transtracheal aspirations (TTA) were carried out in seven patients admitted with pneumonia. This included *S. aureus* endocarditis in four, enterococcal endocarditis in two and pseudomonas endocarditis in one. The TTA's were smear-positive in all four patients with *S. aureus* endocarditis. Two partially treated patients were culture negative. The TTA showed Gram-negative rods on smear and grew *Pseudomonas aeruginosa* in a case of *Pseudomonas* endocarditis. In two patients with enterococcal endocarditis who were admitted with pneumonia, transtracheal aspirations also were done. In neither instance were organisms seen or cultured.

A simple Gram stain of needle aspirate from various suspected metastatic sites yielded preliminary clues as to the pathogen in 17 patients (65.4 percent).

Discussion

Dr. Mullen of Hamilton, Ontario, was the first to draw the attention of Osler to the skin lesions in endocarditis named after Osler.³ Osler did not report if these lesions were examined for bacteria, but correctly speculated that "they are in all probability caused by minute emboli." Horder (1909) described 150 cases of infective endocarditis of which 26 percent were reported to have enterococcal endocarditis and 7 percent staphylococcal endocarditis.⁵ He noted petechiae in 43 of the 150 (29 percent) cases and saw minute emboli lodged in the arterioles of the skin in all but two cases (these lesions were not cultured). Janeway⁴ also described similar ecchymotic eruptions in endocarditis, but did not examine these lesions for bacteria. Blumer (1926) reported Osler's nodes in 19 out of 48 personally observed cases and stated that the "lesion is not pathognomic of the subacute form of bacterial endocarditis" for they were also noted in acute endocarditis due to *Staphylococcus aureus*.²⁰

Nicolous and Poincloux (1929) studied multiple sections of a singular Osler node in endocarditis, but failed to show bacteria by histopathologic examination.¹⁹ Of 167 patients with

subacute bacterial endocarditis reported by Pankey (1961), 70 percent had petechiae, 11 percent had Osler nodes and 5 percent had Janeway lesions.⁶ They did not report if these lesions were examined for bacteria. Lerner and Weinstein (1966) noted Osler nodes in 23 percent of 57 subacute and none of 43 patients with acute bacterial endocarditis.⁸ It is not known if they have examined these lesions for bacteria. Von Gimmengen and Winkelman (1967) also examined the Osler nodes microscopically in two cases, but failed to find bacteria.²⁰ Louria (1967) and his co-workers recovered *Candida stellatoidea* from Osler nodes in a case of candidal endocarditis, and Gram-positive cocci in a case of staphylococcal endocarditis.⁹ Reyes (1973) and associates reported Osler nodes in acute endocarditis due to *Pseudomonas*.¹⁰ In a recent case report¹¹ of staphylococcal endocarditis, large tender pustules with erythematous bases were observed on toes and right palm; aspirates showed Gram-positive cocci.

Peripheral stigmata other than skin lesions in addict endocarditis have also been cultured by others, and pleural fluids,^{1,8,10} joint fluids^{9,12} and spinal fluids¹⁵ have been positive for microorganisms. Interestingly, most of these isolates were *S. aureus*, infrequently Gram-negative rods or candida. Like us, others have also failed to recover enterococci from these sites.

The popular impression that Osler nodes are sterile^{8,19,20} is not substantiated by well-documented reports. Our experience with 26 consecutively seen patients with addict endocarditis suggests that all skin lesions including Osler nodes and lesions of other extravascular sites are frequently due to septic emboli and, in fact, provide valuable early clues to the diagnosis of staphylococcal endocarditis. Seventeen (65 percent) out of 26 patients in our study had bacteria seen and cultured from skin lesions, subcutaneous abscesses, and transtracheal aspirates or pleural fluids. *All 12 patients with staphylococcal endocarditis had at least one or more smear and culture positive extravascular sites.* Although four of the eight patients with enterococcal endocarditis had these lesions, *none had enterococci seen or cultured from such extravascular sites.* One patient (number 16, Table 1) with enterococcal and *Lactobacillus* endocarditis had Gram-positive rods identified upon aspiration of a skin lesion, but no cocci.

It has been reported that in addicts Staphy-

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lococcus aureus endocarditis develops due to the same phage type as is found in their skin cultures.¹⁶ Therefore, cultures of the skin lesions alone in the absence of positive Gram stains of aspirates of the lesions do not suffice to identify a metastatic lesion. Gram stain of these lesions, to be significant, moreover, should show on direct examination, pus cells and bacteria in greater number than the adjacent skin. Arbitrarily, a lesion that shows several polymorphs and bacteria in every third or fourth high-power field should be regarded as positive. A negative lesion may have polymorphs, but the number of bacteria may be no greater than those found on the adjacent skin or may, at most, show a single bacterium in every fifth high-power field.

In the present study, five of seven patients had positive transtracheal aspirates (TTA). In all instances, the organisms identified were either *S aureus* or Gram-negative rods. No bacteria were found in TTA's done in two patients with enterococcal endocarditis. When associated with pneumonia, TTA's appear to be another useful source for the rapid diagnosis of endocarditis. The yield of positive smears and cultures from other extravascular culture sites (joints, pleural and spinal fluids) are shown in Table 1. This aspect was well elucidated in the literature and will not be discussed.

Staphylococcus aureus and enterococci are the major etiologic agents of endocarditis. Therefore, a penicillin or a semisynthetic penicillin is used with an aminoglycoside before results of culture are available. Our study suggests that staphylococcal endocarditis may be readily distinguished from enterococcal endocarditis by simple Gram stain of the needle aspirates of the peripheral lesions when present. In the past this important aspect of endocarditis was underemphasized. Further, enterococcal endocarditis virtually never involves the tricuspid or pulmonary valves. Several other diagnostic techniques were recommended in the past to detect septicemia in endocarditis (for example, serum teichoic acid

antibody titres,¹⁵ serum buffy coat examination¹⁶ and intraleukocytic bacteria studies¹⁷) but these procedures have not been popular and have never come into common use. None of these procedures are as simple and as quick as a diligent clinical examination and a simple Gram stain.

The frequency of classic subacute bacterial endocarditis is now exceeded by that of addict endocarditis in many large metropolitan areas. We emphasize that Osler nodes, Janeway lesions and other innominate skin lesions do occur just as frequently in acute endocarditis in addicts as in the classic subacute disease. Furthermore, these lesions when present, often provide certain important diagnostic and therapeutic clues.

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